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# Optic nerve sheath diameter as a non-invasive tool to detect clinically relevant raised intracranial pressure in children: an observational analytical study

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## ABSTRACT

**Background** Raised intracranial pressure (ICP) contributes to approximately 20% of the admissions in the paediatric intensive care unit (PICU) in our setting. Timely identification and treatment of raised ICP is important to prevent brain herniation and death in such cases. The objective of this study was to examine the role of optic nerve sheath diameter (ONSD) in detecting clinically relevant raised ICP in children.

**Methods** A hospital-based observational analytical study in a PICU of a tertiary care institute in India on children aged 2–14 years. ONSD was measured in all children on three time points that is, day 1, day 2 and between day 4 and 7 of admission. ONSD values were compared between children with and without clinical signs of raised ICP.

**Results** Out of 137 paediatric patients recruited, 34 had signs of raised ICP. Mean ONSD on day 1 was higher in children with signs of raised ICP (4.99±0.57 vs 4.06±0.40; p<0.01). Mean ONSD on day 2 also was higher in raised ICP patients (4.94±0.55 vs 4.04±0.40; p<0.01). The third reading between days 4 and 7 of admission was less than the first 2 values but still higher in raised ICP patients (4.48±1.26 vs 3.99±0.57; p<0.001). The cut-off ONSD value for detecting raised ICP was 4.46 mm on the ROC curve with an area under curve 0.906 (95% CI 0.844 to 0.968), 85.3% sensitivity and 86.4% specificity. There was no difference in ONSD between the right and the left eyes at any time point irrespective of signs of raised ICP.

**Conclusion** We found that measurement of ONSD by transorbital ultrasound was able to detect clinically relevant raised ICP with an excellent discriminatory performance at the cut-off value of 4.46 mm.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Raised intracranial pressure (ICP) significantly contributes to paediatric intensive care unit admissions. Traditional techniques of ICP measurement are invasive, costly, skill driven and not devoid of complications.

### WHAT THIS STUDY ADDS

⇒ Optic nerve sheath diameter (ONSD) can be used as a non-invasive tool for early identification of clinically relevant raised ICP in children. ONSD cut-off value of 4.46 mm had excellent discrimination to diagnose clinically relevant raised ICP with a sensitivity of 85.3% and specificity of 86.4%.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ When obtaining MRI or invasive ICP monitoring is logistically challenging, particularly in lower-middle-income country settings, bedside ONSD measurement is a reliable tool for early identification and management of raised ICP.

## INTRODUCTION

Raised intracranial pressure (ICP) is a frequently encountered condition among children resulting from a variety of neurological and non-neurological aetiologies. It contributes to around 20% of admissions in the paediatric intensive care unit (PICU).[1] Raised ICP has been identified in 86%–93% of children with acute meningitis, 69% of viral encephalitis, 50% of cerebral malaria and 62.5% of patients with cryptococcal meningitis and it has been associated with a higher risk of early mortality.[2–5] Brain herniation is the primary cause of death in about 70% of children with conditions like Japanese encephalitis[6] so it is important to identify and treat raised ICP in the early course of illness to prevent further progression to brain herniation and death.

Despite the availability of traditional invasive techniques for measuring ICP, these remain unused being costly, skill intensive with a steep learning curve and having inherent risks of infection, haemorrhage and brain injury. Non-invasive techniques for detecting raised ICP are optic nerve sheath diameter (ONSD), transcranial Doppler ultrasonography (USG) and neuroimaging with CT or MRI. Although ONSD measurement offers a non-invasive alternative that imposes a minimal financial burden, is readily available and has a simple learning curve for investigators, it has still not been investigated to its full potential, particularly in children. Most of the

studies in children are small and have used ICP values in children with central nervous system (CNS) insult either in the form of infection or trauma for comparison, rather than clinically relevant signs for early identification of raised ICP.[2 7–10] Also there is a paucity of paediatric studies comparing the ONSD between children with CNS insult and those without CNS insult. To fill this gap, we planned a study with a primary objective to examine the role of ONSD in detecting clinically relevant raised ICP in children admitted to the PICU. We measured the ONSD in all children admitted to the PICU within the first 24 hours and repeated on day 2 and again between days 4 and 7 of admission to determine the difference between the groups treated as raised ICP and as non-raised ICP. The secondary objectives were to achieve the cut-off value of ONSD for diagnosing raised ICP and to evaluate whether ONSD values differ in the right versus left eye in patients irrespective of their ICP status.

## METHODS

### Design

A tertiary care hospital-based observational analytical study.

### Setting

PICU of a tertiary care institute of national importance in India.

### Study participants

In the previous year, 73 (35.2%) of 207 patients admitted to the PICU had neurological diseases like meningitis, encephalitis and intracranial space-occupying lesions. Using the Taro Yamane formula, the sample size was calculated to be 137. We used the complete enumeration method to recruit 137 patients aged between 2 and 14 years. Patients with an expected stay in PICU of less than 48 hours, postoperative neurosurgical cases and patients who had ventriculoperitoneal shunt in situ or any eyeball/optic nerve/orbital pathology such as optic neuritis, optic glioma and retinoblastoma were excluded.

Clinical criteria (Muir's) were used to diagnose and treat raised ICP.[11] Neuroimaging and ophthalmoscopic findings also supplemented this decision-making. Patients were classified to the raised ICP group in the presence of one diagnostic or two major or one major along with two minor criteria. Diagnostic criteria included abnormal motor or verbal response to pain, decorticate or decerebrate posture, cranial nerve palsy (especially III, IV and VI) and abnormal neurogenic respiratory pattern (eg, grunting, tachypnoea, Cheyne-Stokes respiration, apneusis). Major criteria included altered mentation, confusion, fluctuating level of consciousness, sustained heart rate deceleration (decrease more than 20 beats per minute) not attributable to improved intravascular volume or sleep state, age-inappropriate incontinence and minor criteria included vomiting, headache, lethargy or not easily arousable, diastolic blood pressure >90 mm Hg and age <5 years. While ICP catheter placement is considered the gold standard method for measuring raised ICP, it is invasive and associated with multiple risks such as infection and haemorrhage. Moreover, it presents challenges in terms of a steep learning curve and availability. Even in the tertiary care centres in India, invasive ICP monitoring is not routinely performed and decisions for treatment of raised ICP are based on clinical criteria supplemented with neuroimaging and ophthalmoscopic findings. Therefore, clinically relevant raised ICP, requiring specific treatment (anti-raised ICP care bundle) was considered the operational gold standard to determine raised ICP and test the diagnostic accuracy of ONSD to identify such patients.

### Study procedure and measurement of ONSD

Transorbital ultrasonography was performed with SonoSite M-turbo (2010, manufactured in the USA) ultrasonography machine with a 13–6 MHz linear array probe using high-resolution optimisation settings with medium gain, on all selected patients. The USG probe was placed on the eyelids to record the ONSD. The USG probe was placed on the superior and lateral aspect of the orbit with the eyelid closed, after applying gel. The probe was moved medially and slightly caudally until a clear image of the optic nerve with clear-cut well-defined margins became visible. The ONSD was measured 3 mm posterior to the globe in coronal view.[12] In non-cooperative patients, findings were recorded either while they were asleep or by using positive reinforcement. The optic nerve appears as a hypoechoic and tubular structure in the echogenic retrobulbar fat perpendicular posterior to the retina, choroids and sclera of the globe.[13]

For each patient, ONSD was recorded at three time points, first within 24 hours of admission, second 24 hours after the first reading (24–48 hours of admission) and third reading on any day between 4 and 7 of hospital admission (figure 1). On each occasion, three readings were taken from each eye and the mean was calculated. Treatment of raised ICP was decided by the treating team as per the PICU protocol. The treating team was unaware of transorbital USG findings throughout the study. The procedure was performed by single operator AB under the technical supervision of study guide LT. Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

### Statistical analysis

SPSS V.20.0 was used for data analysis. Descriptive statistics were used to describe the demographic details and baseline characteristics of the study groups. Intergroup comparisons for primary and secondary outcomes were done using the $\chi^2$, Student's t-test and Mann-Whitney U test for categorical, parametric and non-parametric data, respectively. The sensitivity and specificity of ONSD for detecting raised ICP were determined using the area under the receiver operating characteristic curve (AUROC). The $p<0.05$ was taken as the level of

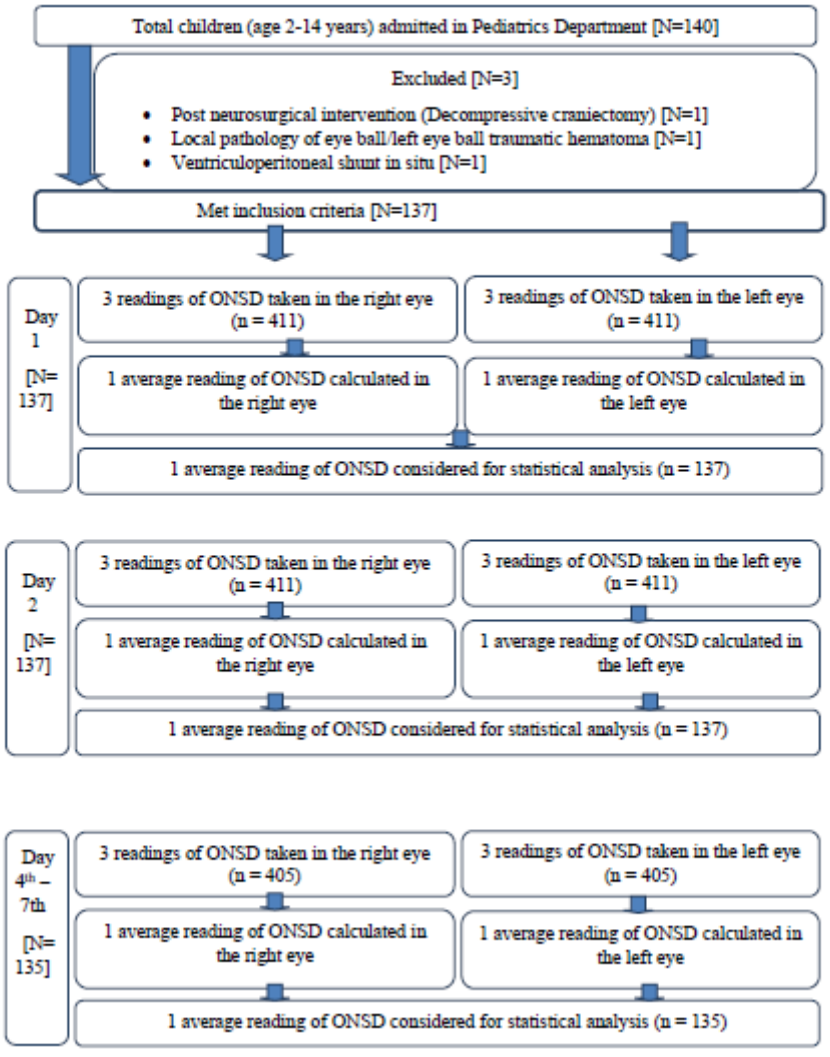


**Figure 1** Flow of data collection and measurement of ONSD. ONSD, optic nerve sheath diameter.

significance. Pearson's correlation coefficient was used to calculate the correlation between two continuous variables.

## RESULTS

### General and demographic data

Out of 137 patients recruited in the study, 34 patients were classified as having raised ICP and 103 patients had normal ICP based on clinical features discussed above. Out of 137 patients, 83 (60.6%) were males and 54 (39.4%) were females. The mean age, height and weight of the participants were 7.77 (SD 3.88) years, 119.6 (SD 24.15) cm and 23.54 (SD 10.4) kilos. None of these was statistically different between the groups (p=0.566, 0.669 and 0.326 for age, weight and height, respectively). The frequency of chief complaints like fever, altered sensorium, seizures and vomiting was statistically different between the two groups. Frequency of generalised tonic-clonic seizures, need for intubation, need for inotropic support, total modified Glasgow Coma Scale of less than 15, sluggish pupillary reaction in either eye, brisk reflex in either knee and absent or extensor plantar response were statistically different between two groups (table 1).

### Comparison of ONSD between raised ICP group and non-raised ICP group

The mean ONSD on day 1 was found to be higher with statistical significance in the patients with raised ICP as compared with those with non-raised ICP (4.99; SD 0.57 vs 4.06; SD 0.40; p<0.001) (table 2). Mean ONSD on day 2 of admission was also higher in raised ICP patients (4.94; SD 0.55 vs 4.04; SD 0.40; p<0.001). The mean ONSD reading recorded between days 4 and 7 was also significantly higher in raised ICP patients (4.48; SD 1.26 vs 3.99; SD=0.57; p<0.001) in comparison to normal ICP patients. As per ROC curve analysis, the cut-off ONSD value for

Table 1 Comparison of chief complaints and clinical events in the first 24 hours of admission at the time of first reading

| Characteristics | Overall (N=137) | Raised intracranial pressure | | P value | OR (95% CI) |
|---|---|---|---|---|---|
| | | Yes (N=34) | No (N=103) | | |
| Chief complaints | | | | | |
| Fever | 77 (56.2%) | 25 (73.5%) | 52 (50.5%) | 0.019 | 0.36 (0.15 to 0.86) |
| Altered sensorium | 25 (18.2%) | 23 (67.6%) | 2 (1.9%) | <0.001 | 0.05 (0.002 to 0.04) |
| Seizures | 21 (15.3%) | 16 (47.1%) | 5 (4.9%) | <0.001 | 0.05 (0.01 to 0.17) |
| Vomiting | 34 (24.8%) | 18 (52.9%) | 16 (15.5%) | <0.001 | 0.16 (0.06 to 0.38) |
| Pain abdomen | 34 (24.8%) | 6 (17.6%) | 28 (27.2%) | 0.264 | 1.74 (0.65 to 4.65) |
| Respiratory distress | 17 (12.4%) | 2 (5%) | 15 (14.5%) | 0.240 | 2.267 (0.596 to 8.615) |
| Anasarca | 14 (10.2%) | 1 (2.9%) | 13 (12.6%) | 0.188 | 3.756 (0.566 to 25.393) |
| Significant clinical events in the first 24 hours of admission in ICU | | | | | |
| Seizures | 22 (16%) | 21 (61.8%) | 1 (1%) | <0.001 | 0.006 (0.001 to 0.04) |
| Intubated/mechanically ventilated | 12 (8%) | 11 (32.4%) | 1 (1%) | <0.001 | 0.02 (0.003 to 0.16) |
| Inotropic support | 15 (10.9%) | 9 (26.5%) | 6 (5.8%) | 0.001 | 0.17 (0.05 to 0.52) |
| Altered sensorium (modified GCS<15) | 38 (27.7%) | 29 (85.3%) | 9 (8.7%) | <0.001 | 0.01 (0.005 to 0.05) |
| Sluggish pupillary reaction | 18 (13.1%) | 17 (50%) | 1 (1%) | <0.001 | 0.01 (0.001 to 0.07) |
| Bilaterally unequal pupillary reaction | 2 (1.4%) | 1 (2.9%) | 1 (1%) | 0.436 | 0.32 (0.02 to 5.31) |
| Brisk Knee Jerk | 34 (24.8%) | 30 (88.2%) | 4 (3.9%) | <0.001 | 0.005 (0.001 to 0.02) |
| Extensor or absent plantar | 33 (24%) | 26 (76.5%) | 7 (6.8%) | <0.001 | 0.02 (0.007 to 0.06) |

GCS, Glasgow Coma Scale; ICU, intensive care unit.

detecting the raised ICP was estimated to be 4.46 mm with a sensitivity of 85.3% and specificity of 86.4%. It had an excellent discriminatory performance with the AUROC of 0.906 (95% CI 0.844 to 0.968) (figure 2).

### Correlation between ONSD values of right and left eyes

There was no difference between the mean ONSD of the right and left eyes at the time of first, second and third reading in all patients irrespective of ICP status (p=0.945, 0.986 and 0.944, respectively). There was an excellent correlation between ONSD values obtained from the right and left eyes at all time points (r=0.994, 0.995 and 0.997) (table 3).

## DISCUSSION

This hospital-based observational analytical study aimed to evaluate the utility of transorbital ultrasonography in measuring ONSD for early detection of elevated ICP. The mean ONSD values were consistently higher in the raised ICP group compared with the non-raised ICP group across all time points, demonstrating statistical significance. Raised ICP was suspected based on chief complaints such as fever, altered sensorium, seizures and vomiting, along with suggestive signs and symptoms. However, to classify a patient in the raised ICP group, we employed objective diagnostic criteria as well as major and minor clinical criteria. In our study, we found no statistically significant differences in the ONSD values between the right and left eyes among patients with raised ICP, those without raised ICP and overall across all patients at different time points.

Table 2 Comparison between mean ONSD readings in both the groups over time

| Sr. no. | Day on which ONSD measured | Mean ONSD in mm (SD) | | P value |
|---|---|---|---|---|
| | | Raised ICP (N=34) | Non raised ICP (N=103) | |
| 1. | Day 1 | 4.99 (0.57) | 4.06 (0.40) | <0.001 |
| 2. | Day 2 | 4.94 (0.55) | 4.04 (0.40) | <0.001 |
| 3. | Day 4th–7th | 4.48 (1.26) | 3.99 (0.57) | 0.02 |

ICP, intracranial pressure; ONSD, optic nerve sheath diameter.

The mean age of study participants in our study was 7.77 years (SD 3.88) with 8.11 years (SD 3.96) in the raised ICP group and 7.66 years (SD 3.87) in the normal ICP group. Mean age, weight and height were not statistically different across both groups. Similar findings were seen by Das *et al* in their study related to age.[10] Sharawat *et al* conducted their study on children aged 2–12 years with 30 patients and 66 healthy controls.[2] Median age was 57 (IQR 33–89) and 51 (IQR 32–86) months in cases and controls, respectively. Padayachy *et al* conducted a study on 174 patients with a median age of 36 months (IQR 8–82).[7] Similar to our findings, they found a good correlation between ONSD values of the right and the left eye (r=0.9, p<0.001).[7]

The mean ONSD on day 1 was higher in the patients with raised ICP (4.99 vs 4.06 mm) in agreement with

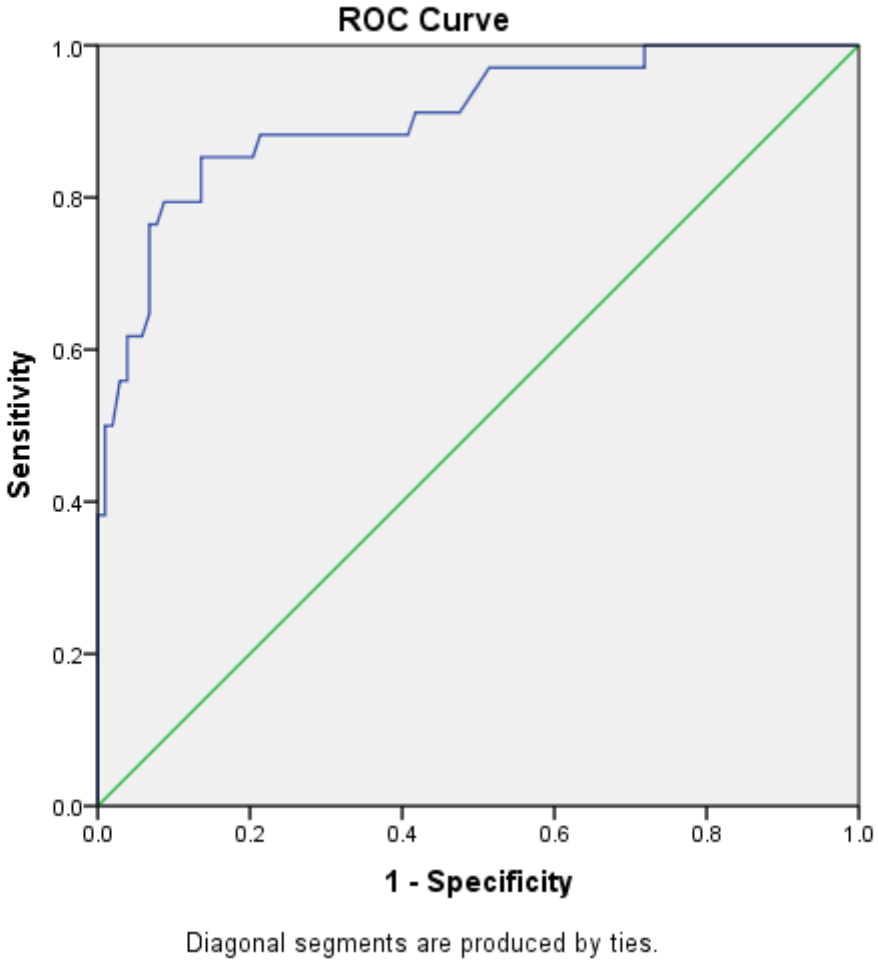


**Figure 2** ROC curve showing the cut-off value of ONSD for detecting raised ICP. ICP, intracranial pressure; ONSD, optic nerve sheath diameter; ROC, receiver operating characteristic.

studies in adults.[14–17] Kimberly *et al* found a strong positive correlation between ONSD and raised ICP with a Spearman rank correlation coefficient of 0.59. They found a mean ONSD of 5.4 mm; SD 0.49 in raised ICP as compared with 4.4 mm; SD 0.49 in patients with ICP<20 cm $H_2O$. Soldatos *et al* found the mean ONSD in

**Table 3** Comparison between mean ONSD readings in both the eyes at the time of the first, second and last reading

| Sr. no. | Day on which ONSD measured | No. of observations (N) | Mean ONSD (SD), mm right eye | Mean ONSD (SD), mm Left eye | P value |
|---|---|---|---|---|---|
| 1. | Day 1 | 822 | 4.290 (0.602) | 4.292 (0.606) | 0.945 |
| 2. | Day 2 | 822 | 4.269 (0.591) | 4.270 (0.592) | 0.986 |
| 3. | Day 4th–7th | 810 | 4.144 (0.744) | 4.148 (0.744) | 0.944 |
| Comparison in raised ICP group | | | | | |
| 4. | Day 1 | 204 | 4.990 (0.570) | 4.997 (0.565) | 0.931 |
| 5. | Day 2 | 204 | 4.949 (0.550) | 4.946 (0.544) | 0.969 |
| 6. | Day 4th–7th | 192 | 4.718 (0.740) | 4.710 (0.735) | 0.938 |
| Comparison in non-raised ICP group | | | | | |
| 7. | Day 1 | 618 | 4.05 (0.39) | 4.06 (0.40) | 0.937 |
| 8. | Day 2 | 618 | 4.04 (0.40) | 4.04 (0.40) | 1.000 |
| 9. | Day 4th–7th | 618 | 4.03 (0.40) | 4.03 (0.41) | 0.820 |

ICP, intracranial pressure; ONSD, optic nerve sheath diameter.

adult patients with moderate brain injury, severe brain injury and in controls as 4.2 mm, 6.1 mm and 3.6 mm, respectively. Geeraerts *et al* found ONSD of 4.9 mm in controls, 5.1 mm in patients with traumatic brain injury (TBI) but normal ICP and 6.3 mm in patients with TBI and raised ICP.

There is a paucity of paediatric data related to ONSD measurements in raised ICP. Our study is one of the largest studies conducted in the field of paediatrics in terms of the number of recordings of ONSD taken and the number of patients recruited. No study has given age-specific values of ONSD in children for detection of raised ICP. Our results agreed with various studies done on paediatric patients.[2 7 10 13 18–20] Sharawat *et al* found the mean ONSD of 5.71 (SD 0.57) mm in the patients with raised ICP, 4.21 (SD 0.66) mm in the patients suffering from CNS diseases but with ICP below 20 mm Hg and 3.71 (SD 0.27) mm in the healthy controls with p<0.001. Das *et al* reported a statistically significant difference in mean ONSD in children with acute liver failure and clinical signs of raised ICP versus those without clinical signs of raised ICP (5.4 mm; 95% CI 4.9 to 5.7 vs 4.6 mm 95% CI 4.1 to 5.3; p 0.01). Malayeri *et al* found a significant difference in mean ONSD (5.6 mm; SD 0.6 vs 3.3 mm; SD 0.6; p<0.001) between the cases with raised ICP and controls in 156 children. Irazuzta *et al* found a mean ONSD of 3.8 mm (SD 0.2) in 13 patients with CSF opening pressure less than 20 cm $H_2O$.

In our study, the AUC for ONSD values reflecting raised ICP was 0.906 (95% CI 0.844 to 0.968). An ONSD value of 4.46 mm for the detection of raised ICP had a sensitivity of 85.3% and specificity of 86.4%. We have compared our cut-off results with various studies done in adults and children (table 4).[2 7–10 14–17 21–25] Differences in the cut-off value of ONSD to diagnose raised ICP across various studies may be due to multiple reasons including age. The aetiology of raised ICP can affect the ONSD values as shown by Padayachy *et al* (craniosynostosis vs intracranial cysts).[7] Moretti and Pizzi showed that other factors can affect ONSD values like placement of USG probes, frequency of doing transorbital USG and the time difference between ONSD measurement and assessment of ICP status.[26]

## Strengths and limitations

Our study includes a large number of observations. We took six readings of each patient on day 1 of admission. A total of 2454 ONSD readings were taken throughout our study, out of which 600 ONSD readings were taken in the raised ICP group. To the best of our knowledge, we took the largest number of observations of ONSD in any paediatric study. We have compared the ONSD values in right versus left eyes to examine any difference due to anatomical reasons. Rather than the numbers indicating ICP, we have used clinical criteria to distinguish raised ICP which is reproducible at any secondary or tertiary care centre though this may be considered a limitation also as we did not measure ICP using invasive catheters. Also, we did not include patients with traumatic raised ICP and our findings are not representative of TBI. Due to different head sizes in children, age-specific values could give a more robust cut-off value for a raised ICP at different ages. Our study does not answer this and

**Table 4** Comparison of sample size, cut-off values of ONSD and their diagnostic value in different studies

| Sr. no. | Author/study | Sample size (n) | Study participants | Cut-off value of ONSD (mm) | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) |
|---|---|---|---|---|---|---|
| 1 | Kimberly *et al*[16] | 15 | Adults | 5 | 88 (47% to 99%) | 93 (78% to 99%) |
| 2 | Moretti *et al*[17] | 63 | Adults | 5.2 | 93.1 (77.2 to 99%) | 73.85 (61.5 to 84%) |
| 3 | Soldatos *et al*[14] | 76 | Adults | 5.7 | 74.1 | 100 |
| 4 | Geeraerts *et al*[15] | 62 | Adults | 5.9 | 87 | 94 |
| 5 | Strumwasser *et al*[25] | 10 | Adults | 6 | 36 | 38 |
| 6 | Rajajee *et al*[23] | 65 | Adults | 4.8 | 96 | 94 |
| 7 | Siranovic *et al*[22] | 20 | Adults | 6.1 | 100 | 83 |
| 8 | Geeraerts *et al*[24] | 37 | Adults | 5.86 | 95 | 79 |
| 9 | Frumin *et al*[21] | 27 | Adults | 5.2 | 83.3 (35.9 to 99.6) | 100 (84.6 to 100) |
| 10 | Padayachy *et al*[7] | 174 | Paediatric | 5.5 | 93.2 | 74 |
| 11 | Rehman Siddiqui *et al*[8] | 8 | <1 year | 3.96 | 100 | 60 |
| | | 21 | 1–10 years | 4.71 | 100 | 63.6 |
| | | 19 | >10 years | 5.43 | 100 | 66.7 |
| 12 | Kerscher *et al*[9] | 72 | Paediatric | 5.57 | 80 | 69.2 |
| 13 | Sharawat *et al*[2] | 30 | Paediatric | 4 | 98 | 75 |
| 14 | Our study | 137 | Paediatric | 4.46 | 85.3 | 86.4 |

ONSD, optic nerve sheath diameter.

we recommend conducting more studies with a larger sample size calculated for this purpose.

## CONCLUSION

ONSD measurement is a useful modality for the early identification of raised ICP in children. We recommend the routine use of transorbital USG to measure ONSD for timely diagnosis of raised ICP in children presenting with altered sensorium or other signs of raised ICP.

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**Contributors** LKT conceptualised and supervised this study and is responsible for the overall content as the guarantor. AB was involved in literature search, data collection and primary draft writing. PK was involved in patient care and drafting. All the authors had access to data, reviewed and approved the final draft of the manuscript.

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**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and the research proposal was approved by the ethics committee of the All India Institute of Medical Sciences, Patna, India vide letter no. AIIMS/Pat/IEC/PGTh/Jan19/19. Participants gave informed consent to participate in the study before taking part.

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**Data availability statement** Data are available on reasonable request.



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